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(54) Title: METHODS AND COMPOSITIONS FOR TREATING AUTOIMMUNE DISEASE

(57) Abstract: The present invention provides methods and compositions for treating auto-immune disease. The methods of the present invention comprise administering to a mammal diagnosed with an auto-immune disease a synergistic ratio of (i) an agent that regulates ICAM-LFA-1 interaction, and (ii) an agent that regulates CD40-CD40 ligand interaction. The compositions of the present invention comprise a synergistic ratio of (i) an agent that regulates ICAM-LFA-1 interaction, and (ii) an agent that regulates CD40-CD40 ligand interaction.

What Is Claimed Is:

1. A method for treating auto-immune disease, said method comprising administering to a mammal diagnosed with said auto-immune disease a synergistic ratio of (i) an agent that regulates ICAM-LFA-1 interaction, and (ii) an agent that regulates CD40-CD40 ligand interaction.

2. The method of claim 1, wherein said agent that regulates said ICAM-LFA-1 interaction and said agent that regulates said CD40-CD40 ligand interaction are administered simultaneously.

3. The method of claim 1, wherein said ICAM is ICAM-1.

4. The method of claim 1, wherein said auto-immune disease is rheumatoid arthritis.

5. The method of claim 1, wherein said auto-immune disease is systemic lupus erythematosis.

6. The method of claim 5, wherein said systemic lupus erythematosis is end-stage disease.

7. The method of claim 1, wherein said agent that regulates said ICAM-LFA-1 interaction is an antibody or an active fragment thereof.

8. The method of claim 7, wherein said antibody is an anti-ICAM antibody or an active fragment thereof.

9. The method of claim 7, wherein said anti-ICAM antibody is an anti-ICAM-1 antibody.

10. The method of claim 1, wherein said agent that regulates said CD40-CD40 ligand interaction is an antibody or an active fragment thereof.

11. The method of claim 10, wherein said antibody is an anti-CD40 ligand antibody or an active fragment thereof.

12. The method of claim 1, wherein said agent that regulates said ICAM-LFA-1 interaction and/or said agent that regulates said CD40-CD40 ligand interaction is a non-antibody agent.

13. A method for treating rheumatoid arthritis, said method comprising administering to a mammal diagnosed with rheumatoid arthritis a synergistic ratio of (i) an antibody that regulates ICAM-LFA-1 interaction, or an active fragment thereof, and (ii) an antibody that regulates CD40-CD40 ligand interaction, or an active fragment thereof.

14. The method of claim 13, wherein said ICAM is ICAM-1.

15. The method of claim 13, wherein said agent that regulates said ICAM-LFA-1 interaction and said agent that regulates said CD40-CD40 ligand interaction are administered simultaneously.

16. The method of claim 13, wherein said antibody that regulates said ICAM-LFA-1 interaction is an anti-ICAM antibody, and wherein said antibody that regulates said CD40-CD40 ligand interaction is an anti-CD40 ligand antibody.

17. The method of claim 16, wherein said anti-ICAM antibody is an anti-ICAM-1 antibody.

18. The method of claim 13, wherein said agent that regulates said ICAM-LFA-1 interaction is an anti-LFA-1 antibody or an active fragment thereof, and wherein said an agent that regulates said CD40-CD40 ligand interaction is an anti-CD40 ligand antibody or an active fragment thereof.

19. The method of claim 13, wherein said agent that regulates said ICAM-LFA-1 interaction and/or said agent that regulates said CD40-CD40 ligand interaction is a non-antibody agent.

20. A method for treating systemic lupus erythematosus, said method comprising administering to a mammal diagnosed with systemic lupus erythematosus a synergistic ratio of (i) an antibody that regulates ICAM-LFA-1 interaction, or an active fragment thereof, and (ii) an antibody that regulates CD40-CD40 ligand interaction, or an active fragment thereof.

21. The method of claim 22, wherein said ICAM is ICAM-1.

22. The method of claim 20, wherein said systemic lupus erythematosus is end-stage disease.

23. The method of claim 20, wherein said agent that regulates said ICAM-LFA-1 interaction and said agent that regulates said CD40-CD40 ligand interaction are administered simultaneously.

24. The method of claim 20, wherein said agent that regulates said ICAM-LFA-1 interaction is an anti-ICAM antibody or an active fragment thereof, and wherein said agent that regulates said CD40-CD40 ligand interaction is an anti-CD40 ligand antibody or an active fragment thereof.

25. The method of claim 6, wherein said anti-ICAM antibody is an anti-ICAM-1 antibody.

26. The method of claim 20, wherein said agent that regulates said ICAM-LFA-1 interaction is an anti-LFA-1 antibody or an active fragment thereof, and wherein said agent that regulates said CD40-CD40 ligand interaction is an anti-CD40 ligand antibody or an active fragment thereof.

27. The method of claim 20, wherein said agent that regulates said ICAM-LFA-1 interaction and/or said agent that regulates said CD40-CD40 ligand interaction is a non-antibody agent.

28. A pharmaceutical composition for treating auto-immune disease, said composition comprising a pharmaceutically acceptable carrier and a synergistic ratio of (i) an agent that regulates ICAM-LFA-1 interaction, and (ii) an agent that regulates CD40-CD40 ligand interaction.

29. The composition of claim 28, wherein said ICAM is ICAM-1.

30. The composition of claim 28, wherein said auto-immune disease is rheumatoid arthritis.

31. The composition of claim 28, wherein said auto-immune disease is systemic lupus erythematosis.

32. The composition of claim 31, wherein said systemic lupus erythematosis is end-stage disease.

33. The composition of claim 28, wherein said agent that regulates said ICAM-LFA-1 interaction is an antibody or an active fragment thereof.

34. The composition of claim 33, wherein said antibody is an anti-ICAM antibody or an active fragment thereof.

35. The composition of claim 34, wherein said anti-ICAM antibody is an anti-ICAM-1 antibody.

36. The composition of claim 28, wherein said agent that regulates said CD40-CD40 ligand interaction is an anti-CD40 antibody.

37. The composition of claim 28, wherein said antibody is an anti-CD40 ligand antibody or an active fragment thereof.

38. The composition of claim 28, wherein said agent that regulates said ICAM-LFA-1 interaction and/or said agent that regulates said CD40-CD40 ligand interaction is a non-antibody agent.

39. The method of claim 1, wherein said synergistic ratio of said agents is administered in the same pharmaceutical composition.

40. The method of claim 13, wherein said synergistic ratio is administered as a composition.

41. The method of claim 20, wherein said synergistic ratio is administered as a composition.

42. The method of claim 1, wherein said method further comprises administering agents other than (i) said agent that regulates ICAM-LFA-1 interaction, and (ii) said agent that regulates CD40-CD40 ligand interaction

43. The method of claim 13, wherein said method further comprises administering agents other than (i) said agent that regulates ICAM-LFA-1 interaction, and (ii) said agent that regulates CD40-CD40 ligand interaction

44. The method of claim 20, wherein said method further comprises administering agents other than (i) said agent that regulates ICAM-LFA-1 interaction, and (ii) said agent that regulates CD40-CD40 ligand interaction

45. A method for treating auto-immune disease, said method comprising administering to a mammal diagnosed with said auto-immune disease a synergistic ratio of (i) a first agent that regulates ICAM-LFA-1 interaction, and (ii) a second agent, wherein said second agent is immunosuppressive and non-cytotoxic.

46. The method of claim 45, wherein said ICAM is ICAM-1.

47. The method of claim 45, wherein said first agent and said second agent are administered simultaneously.

48. The method of claim 45, wherein said auto-immune disease is rheumatoid arthritis.

49. The method of claim 45, wherein said auto-immune disease is systemic lupus erythematosis.

50. The method of claim 49, wherein said systemic lupus erythematosis is end-stage disease.

51. The method of claim 45, wherein said agent that regulates said ICAM-LFA-1 interaction is an antibody or an active fragment thereof.

52. The method of claim 51, wherein said antibody is an anti-ICAM antibody or an active fragment thereof.

53. The method of claim 52, wherein said anti-ICAM antibody is an anti-ICAM-1 antibody.

54. The method of claim 45, wherein said second agent is cyclosporin.

55. The method of claim 45, wherein said agent that regulates said ICAM-LFA-1 interaction is a non-antibody agent.

56. A pharmaceutical composition for treating auto-immune disease, said composition comprising a pharmaceutically acceptable carrier and a synergistic ratio of (i) a first agent that regulates ICAM-LFA-1 interaction, and (ii) a second agent, wherein said second agent is immunosuppressive and on-cytotoxic.

57. The composition of claim 56, wherein said ICAM is ICAM-1.

58. The composition of claim 56, wherein said auto-immune disease is rheumatoid arthritis.

59. The composition of claim 56, wherein said auto-immune disease is systemic lupus erythematosis.

60. The composition of claim 59, wherein said systemic lupus erythematosis is end-stage disease.

61. The composition of claim 56, wherein said agent that regulates said ICAM-LFA-1 interaction is an antibody or an active fragment thereof.

62. The composition of claim 61, wherein said antibody is an anti-ICAM antibody or an active fragment thereof.

63. The composition of claim 62 wherein said anti-ICAM antibody is an anti-ICAM-1 antibody.

64. The composition of claim 56, wherein said agent that regulates said ICAM-LFA-1 interaction is a non-antibody agent.